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Please find attached comments from NICE.

Best wishes
Nick

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NICE Comments: Ombudsman Inquiry on EMA pre-submission activities

The following is in response to the public consultation release, dated 07 October 2018, on "*How the European Medicines Agency engages with medicine producers before they apply for authorisations to market their medicines in the EU - Invitation to comment within the European Ombudsman's inquiry OI/7/2017/KR*".

General Considerations

In addition to responding to the specific questions raised in this inquiry, it is important that the critical role of scientific advice is understood. For transparency, it is also important to note that NICE, through the NICE Scientific Advice service, collaborates with the European Medicines Agency (EMA) and European health technology assessment (HTA) organisations in the delivery of parallel regulatory and HTA scientific advice to the life sciences industry.

Scientific advice helps companies to understand how to design efficient clinical trials and generate robust scientific data to answer questions about the effectiveness and value of their products. It is an essential tool for enabling constructive and structured dialogue between regulatory and HTA (in the case of parallel advice) decision making bodies and industry to ensure that product development plans meet the requirements of decisions makers. In this way, scientific advice can facilitate the development of clinically effective, useful and affordable medicines for the benefit of patients.

In considering the EMA arrangements for scientific advice, it is important to ensure that the major benefits of scientific advice are appreciated and that any recommendations would not inadvertently damage the uptake of scientific advice by life sciences companies. It is also essential to ensure that sound governance processes are in place for scientific advice procedures.

Below are NICE responses to the specific questions raised in the inquiry.

Inquiry Questions

Number	Question
1	It may happen that EMA staff members and experts who participate in pre-submission activities will be involved in the subsequent *scientific evaluation and/or marketing authorisation* procedure for the same medicine. To what extent is this a matter of concern, if at all? Are there specific pre-submission activities of particular concern in this regard? How should EMA manage such situations?
2	Should EMA allow experts from national authorities, who have previously provided scientific advice at national level on a particular medicine, to be involved in EMA's scientific evaluation of the same medicine?
3	What precautionary measures should EMA take to ensure that information and views provided by its staff members and experts in the context of pre-submission activities are not, in practice, considered as a "binding" pre-evaluation of data used to support a subsequent application for authorisation?
4	Is the way in which EMA engages with medicine developers in pre-submission activities sufficiently transparent? If you believe that greater transparency in pre-submission activities is necessary, how might greater transparency affect: i. EMA's operations (for example the efficiency of its procedures, or its ability to engage with medicine developers), and ii. Medicine developers?
5.1	Is there a need, in particular, to enhance the transparency of scientific advice EMA provides to medicine developers? Would it, in your opinion, be useful or harmful, for example, if EMA: - disclosed the names of the officials and experts involved in the procedures;
5.2	- disclosed the questions posed in scientific advice procedures; and/or
5.3	- made public comprehensive information on the advice given.
6	What would the advantages and disadvantages be of making scientific advice, given to one medicine developer, available to all medicine developers?
7	Should EMA be limited to providing scientific advice only on questions not already addressed in its clinical efficacy and safety guidelines [4]?
8	Any other suggestions on how EMA can improve its pre-submission activities?

Comments on Questions Raised

Question	Comment
1.	EMA staff members and experts who participate in pre-submission activities and who are involved in the subsequent scientific evaluation and/or marketing authorisation procedure for the same medicine is a potential concern. With full transparency of the EMA scientific advice procedure and a robust conflicts of interest policy, it may be possible to manage these concerns satisfactorily. Alternatively, scientific advice and market authorisation opinions could be delivered by two separate teams, in order to avoid this issue. Practical issues such as cost, efficiency and availability of expertise would need to be balanced against the benefits of avoiding this issue.
2.	We consider that experts who have previously provided advice at national level on a particular medicine should not generally be involved during the scientific evaluation stage of the same medicine. There may be exceptional circumstances, where for example the expert has advanced expertise not available from other sources. In such situations, opinions by clinical experts should only be allowable after appropriate disclosure and resolution of any conflict of interest issues.
3.	Precautionary measures can include the implementation of clearer and more encompassing guidelines on liability (e.g. a disclaimer labelling the advice as non-binding both for the company and for the EMA), along with appropriate guidance on information disclosure.
4.	There should be full transparency of the EMA scientific advice procedure. It is essential, however, that the scientific advice to individual companies on individual products is undertaken in a safe environment to allow full and open discussion of the key clinical and technical issues. Confidentiality is important in achieving the required safe environment. Additionally, scientific advice engagements will include the consideration of highly sensitive commercial information that could not be released publicly. It is very important that efforts to improve transparency do not have the unintended impact of making scientific advice less attractive to life sciences companies. Where trends emerge from scientific advice engagements with individual companies, and it becomes clear that advice on topics to multiple companies would be appropriate, these topics could form the basis of EMA guidance documents that would be publicly available. The opportunity to seek confidential scientific advice on particular questions should still be made available to companies despite the existence of such guidance documents.

5. For the reasons outlined in our response to Q4 above, we consider that there are good reasons to allow confidential engagements between the EMA and companies on specific proprietary products.

6. Making advice given to one developer available to other developers would fundamentally change the approach to scientific advice and without major safeguards, would most likely make it less attractive to life sciences companies. We consider a better model for providing advice of interest to multiple developers to be through EMA guidance documents as outlined in our response to Q4 above.

7. Scientific advice should not be limited to only questions not already addressed in the EMA clinical efficacy and safety guidelines. This would be overly restrictive and prevent discussion of product specific complexities and nuances in areas covered by the guidelines.

8. NICE considers that the scientific advice provided by EMA is essential in supporting life sciences companies in developing clinically effective, useful medicines for the benefit of patients. Most aspects of the current procedures are viewed as effective and it is important that further developments strengthen scientific advice. Improvements in transparency and governance would be welcome as long as potential unintended consequences are carefully considered and managed.

We hope that our response to the inquiry is helpful. Please do not hesitate to contact me by emai [redacted] if any clarification is needed.

Kind regards,
Dr Nick Crabb, Programme Director, Scientific Affairs

21/01/2019